

graph showed an additive effect rather than a synergistic effect of the aspirin and vitamin.

On June 2, 1994, the Examiner granted the undersigned a telephone conference for which Applicant thanks the Examiner. During that telephone conference, the undersigned noted that the lack of clarity in the graph was as a result of faxing the graph to England for the signature of the Affiant, Dr. Larry Hollier. Applicant suggested that a more detailed graph be submitted so that the Examiner could see the actual synergistic effect of Applicant's combination. Accordingly, Applicant submits herewith a full color graph attached hereto which graphically shows the relative risk reductions associated with aspirin and vitamin use for men, taken from Table 3 of the application.

The graph plots the information on the attached table which shows the change in relative risk reduction of heart disease in men taken from Table 3 of the application with 1 as the base line for men using neither aspirin nor vitamins. As can be seen from Table 3 of the application, men who use vitamins alone showed a .02 increase in all deaths. Since there was no relative risk reduction, but instead a relative risk increase, the attached table shows a negative change of .02 for all deaths for men who used vitamins only. Similarly, Table 3 shows a relative risk of all deaths for men using aspirin only as 1. Since 1 is the base line, the accompanying table shows no change in relative risk reduction for all deaths for men using aspirin only. Accordingly, the anticipated combination of the use of vitamin alone and

aspirin alone would be a negative .02 (.02 + 0), that is, a relative increase in all deaths anticipated for men taking both vitamins and aspirin. Accordingly, it would not be obvious to one of ordinary skill in the art to use such a combination to combat all deaths, when such a combination would be anticipated to increase the number of deaths. Table 3 shows, however, that the actual relative risk reduction for men using both aspirin and vitamins is .91 which is a change of .09 from the baseline, which translates into a .09 change in relative risk reduction as shown in the attached table.

This information can be seen from the first set of columns on the attached graph which shows, for all deaths, a slight decrease in relative risk reduction for the use of vitamins only, no difference for the use of aspirin only, an anticipated slight increase in relative risk for the combination of the two, and a substantial relative risk reduction for all deaths for the actual combination of vitamin and aspirin. Similar results can be seen for all deaths, total cardiovascular deaths, myocardial infarctions, ischemic heart disease, and other heart disease. The graph clearly shows that the anticipated combination, that is the anticipated additive effect of vitamin use combined with aspirin use, is far less than the actual synergistic results from the combination of vitamin and aspirin. Accordingly, the combination of vitamin and aspirin shows a marked synergy far in excess of even the anticipated additive effect of vitamin use with aspirin use.

Based on the foregoing, Applicant respectfully submits that its claims 11-26 show a distinct synergy not anticipated by the individual effects of the

separate components. Applicant submits that claims 11-26 are, therefore, in condition for allowance at this time, patentably distinguishing over the cited prior art. Accordingly, reconsideration of the application and passage to allowance are respectfully solicited.

Applicant will follow up this Communication with a telephone call to the Examiner to address any questions or concerns the Examiner may have in interpreting the attached tabular and graphic representations of the data from Table 3 of the application.

Respectfully submitted,

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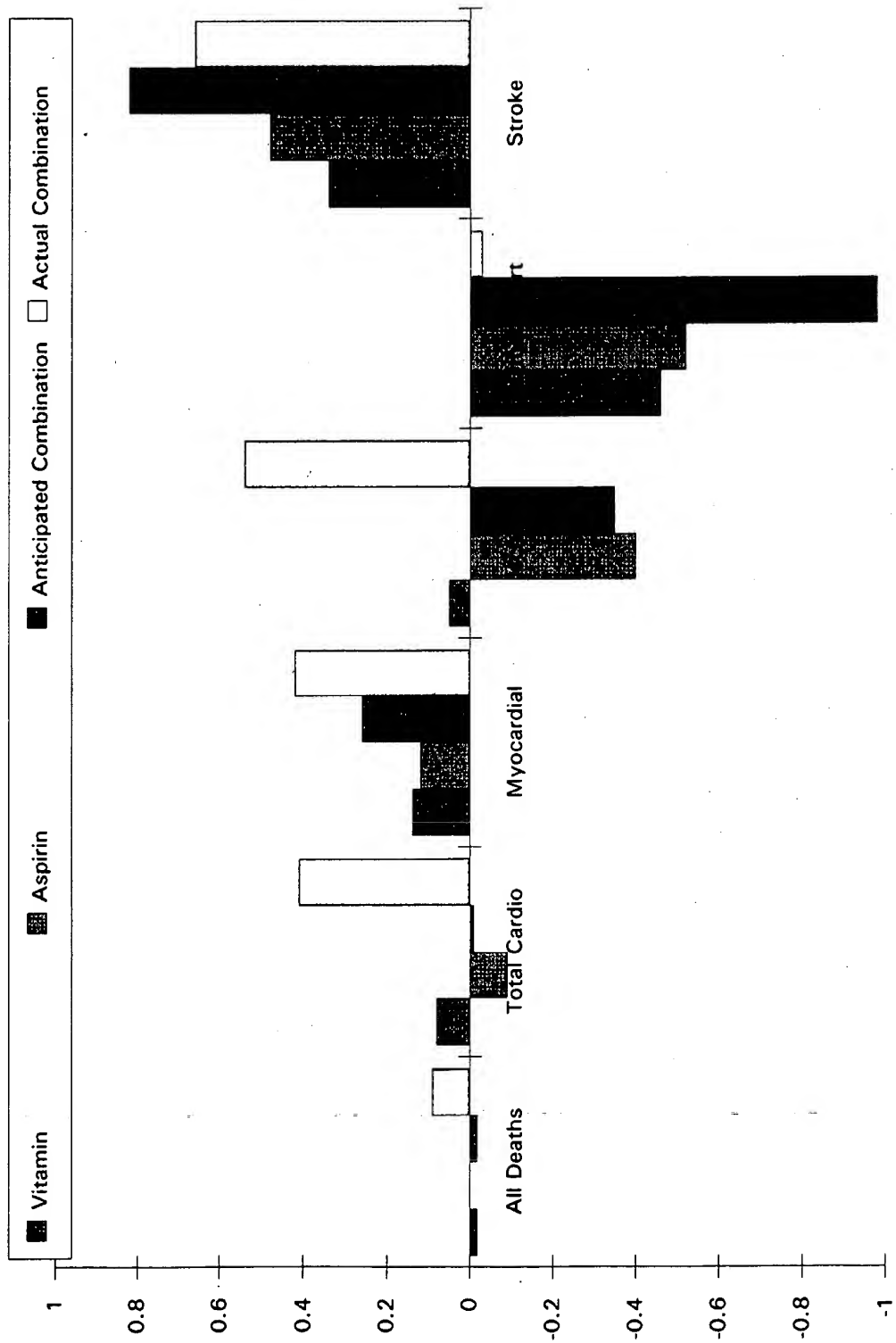
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KREAMER.XLS Chart 2



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